REMARKS

The Present Invention

The present invention pertains to a water-soluble compound, a composition thereof, a method of treating cancer with the water-soluble compound, and a method of preparing a water-soluble compound.

The Pending Claims

Claims 63, 65, 66, 68-70, 72, 73, 75-77, 79-81, 83-87, 90 and 91 are currently pending. Claims 63, 65, 66, 68-70 and 72 are directed towards the water-soluble compound. Claims 73, 75 and 76 are directed towards the composition comprising the water-soluble compound. Claims 77, 79 and 80 are directed towards the method of treating cancer with the water-soluble compound. Finally, claims 81, 83-87, 90 and 91 are directed towards the method of preparing a water-soluble compound.

Amendments to the Claims

The claims have been amended to point out more particularly and claim more distinctly the present invention. In particular, claims 63 and 81 have been amended to recite that X is an amino acid residue, a peptide residue, a polypeptide residue, or a protein residue, as supported by the specification at, for example, page 10, lines 14-21 and page 32, lines 8-23. Claim 68 has been amended to recite that the polar moiety is L-cysteinyl, as supported by the specification at, for example, page 10, lines 22-27 and Example 1. No new matter has been added by way of these amendments.

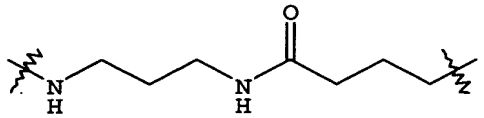
Summary of the Office Action

The Office alleges that the claims still include non-elected subject matter and require further restriction. Claims 63, 65, 66, 68-70, 72, 73, 75-77, 79-81, 83-87, 90 and 91 have been rejected as being drawn to an improper Markush group. Claims 63, 65, 66, 68-70, 72, 73, 75-77, 79-81, 83-87, 90 and 91 have been rejected under 35 U.S.C. § 112, second paragraph, as allegedly indefinite. Finally, the Office has rejected claims 77, 79 and 80 under 35 U.S.C. § 112, first paragraph, as allegedly non-enabled. Reconsideration of the pending claims is respectfully requested.

Discussion of the Election/Restriction and Improper Markush Rejection

According to the Office, claims 63, 65, 66, 68-70, 72, 73, 75-77, 79-81, 83-87, 90 and 91 lack unity of invention, since residues A and X are defined in such a way that the

core compound keeps changing. Applicants submit that the Office Action issued June 3, 2002 set forth a restriction requirement that required election of a group and a species from that group. The Office Action states, "Further, Applicant is required, in reply to this action, to elect a single species, falling within the elected group, to which the claims shall be restricted if no generic claim is finally held to be allowable...Upon allowance of a generic claim, applicant will be entitled to consideration of claims to additional species which are written in dependent form or otherwise include all the limitations of an allowed generic claim as provided by 37 CFR 1.141" (see page 3 of Office Action). In the response filed June 28, 2002, Applicants elected Group I (i.e., claims 63-80), requested examination of Group II (i.e., claims 81-91) in conjunction with Group I, and elected the species in which A is Geldanamycin, the spacer moiety (i.e., B_1-B_2) has the structure



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and X is L-cysteine. This specie was elected *for search purposes only*, and Applicants do not believe that further amendment of the claims is necessary. In view of the foregoing, this rejection should be withdrawn.

Discussion of the Section 112, second paragraph, Rejection

The Office has rejected claims 63, 65, 66, 68-70, 72, 73, 75-77, 79-81, 83-87, 90 and 91 as allegedly indefinite, since the polar moiety X is selected from a group of compounds and not substituents with open valencies. The claims have been amended to recite wherein X is an amino acid residue, a peptide residue, a polypeptide residue, or a protein residue. One of ordinary skill in the art would understand that, for example, a compound in which X is an amino acid implies that X is a residue with an open valency, such as, L-cysteinyl or L-lysinyl. The compounds recited in the pending claims and specification clearly indicate that the sulfur moiety contains a bond attaching to an open valency on the residue X.

In addition, the Office contends that claims 63, 65, 66, 68-70, 72, 73, 75-77, 79-81, 83-87, 90 and 91 are indefinite because the point of attachment is not indicated for the moieties provided for X. Applicants submit that one having ordinary skill in the art would readily be able to determine possible points of attachment in view of the specification and chemistry that is well known in the art. The only prerequisite for the amino acid residue, peptide residue, polypeptide residue or protein residue of X is that it contains at least one nucleophilic group (e.g., the thio group on a L-cysteine) capable of forming a compound as

taught by the specification. The specification provides examples of preparing suitable compounds of the invention at, for example, page 33, line 31, through page 40, line 30.

Therefore, in view of the amendments and the foregoing discussion, the pending claims are clear and definite, and the rejection is believed to be moot.

Discussion of the Section 112, first paragraph, Rejection

The Office has rejected claims 77, 79 and 80 under Section 112, first paragraph, as allegedly not enabled. In particular, the Office contends that the specification does not provide an adequate representation regarding which types of cancers express Hsp90. This rejection is without merit.

Specific cancers that express Hsp90 were known in the art at the time the patent application to which the subject patent application claims priority (U.S. Application No. 60/093,284) was filed, i.e., July 17, 1998. For example, Nanbu et al., *Cancer Detect. Prev.* 22(6): 549-555 (1998), teaches that Hsp90 expression is common to endometrial carcinomas, including cancers of the uterus, ovaries, and/or prostate. Furthermore, Franzen et al., *Electrophoresis* 18(3-4): 582-587 (Mar-Apr 1997) and Yano et al., *Jpn. J. Cancer Res.* 87(9): 908-915 (1996), disclose that the expression of Hsp90 was higher in breast cancer cells compared to healthy tissue. Moreover, Kojika et al., *Leukemia* 10(6): 994-999 (1996) and Xiao et al., *J. Tongji Med. Univ.* 16(4): 212-216 (1996), disclose that leukemic tissue, including acute lymphoid leukemia, acute non-lymphoid leukemia, and myelodysplastic syndrome, showed an enhanced expression of Hsp90 compared to healthy tissue. Other references cite similar findings in which Hsp90 is expressed in various types of cancer, including gastrointestinal cancers (e.g., gastric, pancreatic, colon), tumors of the central nervous system, and tongue carcinomas (see, for example, Ehrenfried et al., *Surg. Oncol.* 4(4): 197-203 (1995); Kato et al., *Acta Neuropathol. (Berl)* 89(2): 184-188 (1995); Ito et al. *J. Oral Pathol. Med.* 27(1): 18-22 (Jan. 1998); and Thomas et al. *Br. J. Urol.* 77(3): 367-372 (1996)). The abstracts of these references are attached hereto. Accordingly, those having ordinary skill in the art would readily be able to use the presently inventive compounds to treat cancer that expresses Hsp90 in view of the specification and known information at the time of filing.

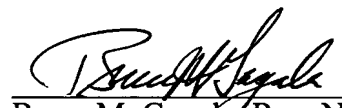
Furthermore, Applicants point out that under Section 112 they need not, and preferably do not, disclose in the specification what is known in the art under Section 112. In *In re Johnson*, 127 U.S.P.Q. 216 (C.C.P.A. 1960), for example, it was held that the claimed compound was reasonably enabled as an insecticide and fungicide despite the absence of disclosure of any particular concentrations to be used or the particular kinds of insects or fungi to be treated because "these are matters which could be expected to be

within the knowledge of a person of ordinary skill in the art." Accordingly, Applicants have enabled a method of treating cancer in a mammal in view of the exhaustive prior art literature regarding what types of cancers express Hsp90. Therefore, Applicants respectfully request the withdrawal of this rejection.

Conclusion

The application is considered to be in good and proper form for allowance, and the Examiner is respectfully requested to pass this application to issue. If, in the opinion of the Examiner, a telephone conference would expedite the prosecution of the subject application, the Examiner is invited to call the undersigned attorney.

Respectfully submitted,



Bruce M. Gagala, Reg. No. 28,844
LEYDIG, VOIT & MAYER, LTD.
Two Prudential Plaza, Suite 4900
180 North Stetson
Chicago, Illinois 60601-6780
(312) 616-5600 (telephone)
(312) 616-5700 (facsimile)

Date: May 22, 2003